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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,108	12/10/2004	Lai-Xi Wang	014835-187.02-002	3314
24239 7590 08/06/2008 MOORE & VAN ALLEN PLLC P.O. BOX 13706 Research Triangle Park, NC 27709				
EXAMINER				
LEWIS, PATRICK T				
ART UNIT		PAPER NUMBER		
1623				
MAIL DATE		DELIVERY MODE		
08/06/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/518,108

Applicant(s)

WANG ET AL.

Examiner

Patrick T. Lewis

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 11, 15, 19, 25, 26, 28, 29 and 37 is/are pending in the application.
- 4a) Of the above claim(s) 11, 15, 19, 25, 26, 28, 29 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on December 10, 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on September 13, 2007 is acknowledged. The requirement was made FINAL in the Office Action dated September 27, 2007.
2. Claims 11, 15, 19, 25-26, 28-29 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant's Response Dated December 27, 2007

3. Claims 1-4, 11, 15, 19, 25-26, 28-29 and 37 are pending. An action on the merits of claims 1-4, 11, 15, 19, 25-26, 28-29 and 37 is contained herein below.
4. The objection to claim 10 has been rendered moot in view of applicant's amendment dated April 25, 2008.
5. The rejection of claims 1-4, 9-10 and 16 under 35 U.S.C. 112, first paragraph, has been rendered moot in view of applicant's amendment dated April 25, 2008.
6. The rejection of claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Brask et al. Journal of peptide Science (2000), Vol. 6, pages 290-299 (Brask) and Nefzi et al. Tetrahedron Letters (1995), Vol. 36, pages 229-230 (Nefzi) in combination is maintained for the reasons of record as set forth in the Office action dated September 27, 2007.

7. The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Brask et al. Journal of peptide Science (2000), Vol. 6, pages 290-299 (Brask) and Nefzi et al. Tetrahedron Letters (1995), Vol. 36, pages 229-230 (Nefzi) in combination has been rendered moot in view of applicant's amendment dated April 25, 2008.

Rejections of Record Set Forth in the Office Action Dated September 27, 2007

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brask et al. Journal of peptide Science (2000), Vol. 6, pages 290-299 (Brask) and Nefzi et al. Tetrahedron Letters (1995), Vol. 36, pages 229-230 (Nefzi) in combination.

Claims 1-4 are drawn to a maleimide cluster comprising at least one core carbohydrate molecule wherein at least two or more maleimides are attached to the core and optionally comprising a protein.

Brask teaches multifunctional, topological template molecules such as linear and cyclic peptides have been used for the attachment of peptide strands to form novel protein models (Abstract). The concept of carbohydrates as templates for de novo design of potential protein models has been previously described and these novel chimeric compounds were termed carbopeptides. (page 290) To bypass the problematic folding step of linear polypeptides, Mutter and coworkers have suggested a template-assembled synthetic proteins (TASP) concept which relies on a multifunctional topological scaffold or template, which enhances the spatial accommodation of the

peptides. Carbohydrates are promising candidates for templates for the display of functional groups due to their inherent multifunctionality, the relative rigidity of ring forms, ease of regioselective chemical manipulations, and access to stereoisomers of mono- and disaccharides (page 291). The preparation of carbopeptides by oxime ligation is shown in Figures 2-5. In a model study, 2,4-dimethoxybenzaldehyde was coupled to methyl 2,3,4,6-tetra-O-Ac- α -D-Galp (7) at room temperature (page 296).

Brask differs from the instant invention in that Brask does not teach a TASP containing maleimide functions; however, it would have been obvious to one of ordinary skill in the art at the time of the invention to do so in view of the teachings of Nefzi.

Nefzi teaches a method of chemoselective ligation for TASP synthesis using the maleimide function, which is known to react rapidly and rather selectively with thiols (page 229). This should allow for the condensation of peptides containing a thiol group to template molecules containing the maleimide function. Applicant's attention is directed to Scheme 1 wherein Nefzi shows a maleimide function covalently attached to a template which is then reacted with a thiol-containing peptide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to attach peptides to a maleimide function covalently linked to a template. One would have been motivated to incorporate a maleimide function because they are known to react rapidly and rather selectively with thiols. It would have also been obvious to one of ordinary skill in the art to select a monosaccharide as the template. As taught by Brask, carbohydrates are promising candidates for templates for the display of functional groups due to their inherent multifunctionality, the relative rigidity of

ring forms, ease of regioselective chemical manipulations, and access to stereoisomers of mono- and disaccharides.

10. Applicant's arguments filed April 25, 2008 (December 25, 2007 have been fully considered but they are not persuasive. Applicant argues that Brask requires linkers in its synthetic proteins in order to create moveable arms within the final structure. Applicant contends that flexibility is an important characteristic of the Brask molecules which is in stark contrast to the rigid structure of the molecules described in Nefzi. Applicant further asserts that if the carbohydrate core, with or without movable arms, of Brask is introduced into the Nefzi structure, then the required rigidity of the Nefzi structure is lost.

The examiner respectfully disagrees with applicant's assertions and characterization of the prior art. Brask and Nefzi both employ Template Assembled Synthetic Proteins (TASP) to bypass the so-called protein folding problem. In this approach, peptide blocks with inherent secondary structure are attached to a topologically defined template, which promotes their folding into a distinct tertiary structure. Neither Brask nor Nefzi teach direct attachment of the peptide to the "template". Brask teaches the use of a "linker" to attach the peptide to the "template". Nefzi teaches the attachment of the peptide to the "template" by using four maleimide functions (a "linker").

Although Nefzi describes the use of generic "templates", Brask teaches that carbohydrates are promising candidates for templates for the display of functional groups due to their inherent multifunctionality, the relative rigidity of ring forms, ease of

regioselective chemical manipulations, and access to stereoisomers of mono- and disaccharides (page 291). As discussed by Brask, the development of techniques for chemoselective ligation of unprotected peptide segments has significantly extended the reach of synthetic peptide chemistry. Common to these methods is the chemoselective reaction of two mutually reactive functionalities, one on each segment. Some methods rely on the formation of a non-natural bond at the site of ligation, this includes oxime and hydrazone ligations. With aldehydes and ketones oximes are formed which are stable under neutral to mildly acidic conditions. Other chemoselective reactions are thioether and thioester ligations, based on reactions between a thiol or thioacid nucleophile and a bromoacetyl moiety.

Thus, the selection of appropriate functionalities to attach the "template" and peptide would have been well within the purview of the skilled artisan at the time of the instant invention. Nefzi teaches a method of chemoselective ligation for TASP synthesis using the maleimide function, which is known to react rapidly and rather selectively with thiols (page 229). This should allow for the condensation of peptides containing a thiol group to template molecules containing the maleimide function. Applicant's attention is directed to Scheme 1 wherein Nefzi shows a maleimide function covalently attached to a template which is then reacted with a thiol-containing peptide. Simple substitution of one known element (i.e., a specific "linker" or "template") for another to obtain predictable results renders the instant invention obvious in view of the teachings of the prior art.

Conclusion

11. Claims 1-4, 11, 15, 19, 25-26, 28-29 and 37 are pending. Claims 1-4 are rejected. Claims 11, 15, 19, 25-26, 28-29 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dr. Patrick T. Lewis/
Primary Examiner, Art Unit 1623

ptl